

CONCLUSIONS.—1. There are three main types of primary carcinoma of the lungs which present characteristic gross pathological appearances: the infiltrative, the miliary, and the mixed.

2. The roentgen examination and the stereoscopic study of roentgenograms will early point to a pulmonary lesion and its probable nature.

3. The areas of increased density found in primary pulmonary carcinoma are usually quite typical, and can be differentiated from areas of increased density caused by other diseases in the thorax, including inflammatory changes and neoplasms, both primary and metastatic.

4. A careful correlation of the roentgen findings with the clinical history and the physical and laboratory findings usually makes a clinical and differential diagnosis possible.

REFERENCES.

1. Adler, I.: Primary malignant growths of the lungs and bronchi, a pathological and clinical study. London, Longmans, 1912.
2. Moore, A. B.: Roentgen diagnosis of bronchiectasis. Am. Jour. Roent., 1910, iii, 524.
3. Moore, A. B., and Carman, R. D.: Radiographic diagnosis of metastatic pulmonary malignancy, a report of seventy-one cases. Am. Jour. Roent., 1910, iii, 126-131.

A STUDY OF SIXTY-TWO CASES OF DIABETES OF FIFTEEN OR MORE YEARS' DURATION.

BY ALBERT A. HORNOR, M.D.,

AND

ELLIOTT P. JOSLIN, M.D.,

BOSTON, MASSACHUSETTS.

IN 1912 among the 394 cases of diabetes traced out of 505 cases seen 17 per cent. had lived ten years or more, and if the large number of living patients who had acquired their diabetes less than ten years previously was subtracted the percentage of patients living ten or more years rose to 26 per cent. Now that five years have elapsed it has seemed desirable to again review our series of cases, but this time to discuss those patients who have survived their diabetes not alone ten but rather fifteen years. A sufficiently large number of such patients are available to make this investigation worth while, for the list contains 62 individuals. This number constitutes 6 per cent. of the total cases of diabetes traced up to the present time, but if we deduct from it those living cases whose onset occurred more recently than fifteen years ago the percentage of diabetics who have survived fifteen or more years from the onset of the disease rises to 11 per cent.

The duration of life of diabetics, however, is by no means limited to fifteen years, for among the 62 cases here discussed 37 are still

alive, and the average length of life for the total 62 cases up to December 1, 1916, was nineteen years and seven months. In the two following diagrams the duration of life of the living cases up to December 1, 1917, and of the fatal cases has been arranged according to the decade of age at onset.

These tables show that prolonged diabetes in the young is exceedingly rare. Indeed, there is only one case whose age at onset was less than ten years. This is Case No. 887, who showed at autopsy, according to Dr. J. E. Ash, a congenital deficiency of the pancreas. In the second decade there are 2 cases, one living and one dead. Case No. 1153, who is living, is one for whom many might challenge a diagnosis of diabetes, but although he has been many months at a time without having sugar demonstrated in the urine, glycosuria occurs whenever the diet is broken. Reference to this case will be made later, because this exceptional patient failed to show obesity.

Males constituted 55 per cent. of the 62 cases, and this proportion is nearly as high as that for the total cases of our series (60 per cent.). It is certainly an interesting fact that more males are treated for diabetes according to the diabetic authors, but that according to national statistics more women succumb to the disease.

The discovery of the disease was made quite independently of the appearance of symptoms in 17 of the cases. Thus, 12 patients, or 19 per cent., learned of their condition at examination for life insurance and 5 others upon the occasion of a periodic medical examination. The importance of life insurance examinations in this series becomes evident when one compares its incidence among these fifteen-year cases of 19 per cent. with the 6 per cent. incidence of insurance among the entire number of our cases available for this purpose; thus among the fifteen-year cases those discovering the disease by insurance were three times as frequent as was the rule for the total number of diabetics.

The predisposing factors in the etiology were few. Obesity heads the list, for it was present in 60 out of 62 cases; an hereditary or familial tendency existed in 21, or 34 per cent., in contrast to 21 per cent. for all of our cases; worry obviously existed in 9 and trauma also in 9, dietary excesses in the form of sweets in 8 and lues in 4. Two were cases of pregnancy and 8 of the patients obviously had gall-stones.

Obesity, here as elsewhere in diabetes, far outranks all other etiological factors. All the women were obese and all but two of the men. In one of these two exceptional cases the onset was at eighteen years of age. The patient (Case No. 1153) had been a very sickly child, with frequent attacks of cyclic vomiting. The other patient, Case No. 1060, was an hereditary case of diabetes, and later developed tuberculosis and nephritis. The importance of obesity was also recognized in the paper upon the cases of ten years' duration, and, in fact, 26 of the 67 patients then studied had weighed, at

some time or other, over 200 pounds. The more carefully our records are gathered the more frequently is obesity proved to precede the onset of diabetes. Naunyn makes the same remark regarding heredity. The degree of obesity which occurred in these 62 diabetics is graphically shown in the accompanying chart.

TABLE I.—FATAL CASES OF DIABETES OF FIFTEEN OR MORE YEARS' DURATION ARRANGED ACCORDING TO DECADE OF ONSET.
DURATION IN YEARS.

AGE AT ONSET	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	TOT. ALB.
61-70		1	1					1														3
51-60	2	1		1	1	3																8
41-50	1	3	2		1	1					1											9
31-40				1				1														2
21-30																						1
11-20							1															1
0-10																1						1
TOTALS	3	5	1	1	2	4	2	1			1					1				1	25	

A familial or hereditary history of diabetes was obtained in 21, or 34 per cent., of these fifteen-year cases. This should be compared with the incidence of heredity, amounting to 25 per cent., in the ten-year group of our cases and the 27 per cent. of heredity which exists among those of Jewish extraction.

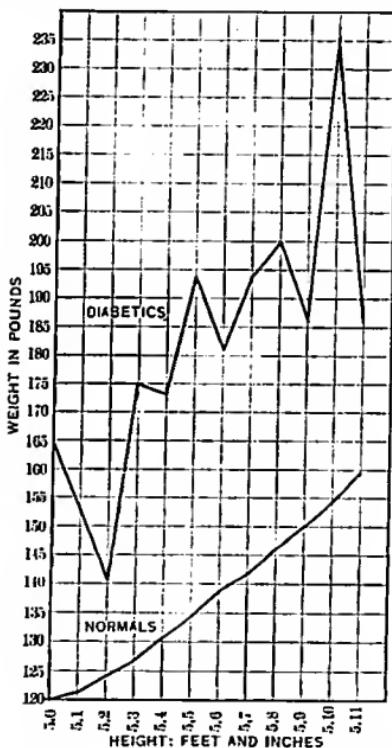
TABLE II.—LIVING CASES OF DIABETES OF FIFTEEN OR MORE YEARS' DURATION ARRANGED ACCORDING TO DECADE OF ONSET.
DURATION IN YEARS.

AGE AT ONSET	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	TOT. ALB.
61-70						2																2
51-60	1	1		1	2			1		1												7
41-50	1	2		3	1	2	1				1											11
31-40	3	2	1	1	1	1	1						1			1						12
21-30		2	1	1																		4
11-20				1																		1
0-10																						0
TOTALS	2	6	4	7	5	5	1	3			1	1	1			1						37

The evidence here furnished therefore shows that among cases of diabetes of fifteen years' duration an hereditary and familial history of diabetes reaches its highest mark, but conversely and contrary to our present belief the presence of heredity may not be a favorable prognostic sign, because among our 251 hereditary cases of diabetes only 21, or 8 per cent., lived fifteen years.

Two fifteen-year patients (Cases Nos. 37 and 155) have children with diabetes. One of these children developed the disease at the age of nine years, which was eight years after the onset of the disease in his mother, and today, nine years later, is in good condition and free from sugar. The diabetes in Case No. 37 was of seventeen years' duration and began at the age of forty-five. This was twenty-

CHART I.—DIABETES OF FIFTEEN YEARS' DURATION. A COMPARISON OF THE WEIGHTS OF NORMAL INDIVIDUALS AND OF SIXTY-TWO DIABETIC PATIENTS PRIOR TO THE ONSET OF THE DISEASE.



one year after the birth of her son, who later developed diabetes at the age of forty-one years. It is also interesting that the wife of one of the fifteen-year cases had diabetes prior to its discovery in her husband, and this may account for the fact that he was treated so soon after the onset of the disease.

Trauma as an exciting factor in the onset of the disease among 9 of these patients is cited, but it is too indefinite to warrant conclu-

sions as to its importance, either pro or con. In only 8 of the cases was the overeating of sweets definitely noted. If the records were more complete in this regard the number of such instances might be greater. Smokers should derive consolation and smokers' wives should take warning when they learn that more than once we have been told by men that, following the substitution of candy for tobacco at the solicitation of their wives, weight increased and diabetes developed.

Few cases in our entire series have shown sufficient trouble with the liver to make this a serious factor. There have been three deaths from cirrhosis, and one of these occurred in a fifteen-year patient. About half (29) of the 62 fifteen-year cases presented a palpable liver, but this was usually attributed to the ease of palpation because of emaciation rather than to any demonstrable enlargement of the liver.

The knee-jerks were present in all cases, and in only one were they even noted as diminished. It so happens that this case was the only one who showed an enlarged thyroid. In but a single case did the pupils fail to react. Of course, all of the cases have not been personally examined throughout the entire period of fifteen or more years, but this has been true of a large proportion. The normal pupils, in conjunction with the normal patella reflexes, lend very little support to the idea that long-lasting diabetes leads to the so-called diabetic tabes or that syphilis is common in diabetes.

Cataract was recorded in but 3 cases.

The teeth were noted as good in 19 out of 43 cases. Bad teeth do not necessarily precede diabetes, and by no means necessarily occur during its course, even if the disease is of prolonged duration.

The evidences of arteriosclerosis were numerous. Thus 36 patients showed distinct manifestations, and in only 14 of the 62 cases did we feel confident that the bloodvessels were normal. Gangrene occurred in 9 of the patients, and of these 5 have died. The records of the blood-pressure are meager, due in large measure to the early period at which many of the patients were seen. The systolic blood-pressure exceeded 190 mm. Hg. in 6 cases, ranged between 150 and 190 in a like number, and between 120 and 150 mm. Hg. in 9.

Nephritis was of common occurrence. During this last year special study was made of the renal efficiency of a few of the cases by our fellow-worker, Richard Ohler. He determined the non-protein nitrogen in 10 patients. In one-half of these it was less than 31 mgm., and was thus in harmony with the blood-pressures of this group, which were normal. In the other 5 cases 2 showed 50 mgm., one 40 mgm., and the other two 34 mgm. non-protein nitrogen per 100 c.c. blood. These 5 cases presented other characteristic evidences of extreme nephritis as well, although, strangely enough, all are now living. One, however, is at present in a very

critical condition, due to nephritis. To determine the degree of renal involvement in 2 cases, phenolsulphonephthalein was injected, and the amount excreted in two hours was found to be about 30 per cent.

The fifteen-year cases now living diet more carefully and keep more nearly sugar-free than did those who have died. Of the 37 living cases, 13 very easily became sugar-free, and 11 of these so remain with slight or moderately restricted diet. One case, a pregnancy case (Case No. 309), is even able to eat pure sugar. With rather more restriction 4 cases became sugar-free, but in 3 other cases temporary fasting was employed to attain this end. Five cases became sugar-free with difficulty even with fasting and a very restricted diet. At present a diabetic diet has been abandoned by 2 cases, and 3 patients are obliged to diet very strictly. Nine of the fatal cases were never sugar-free from the time of the first visit until death, but 5 cases were known to be sugar-free at the time of death. Another became free after living five years on a moderately restricted diet. One case became sugar-free easily in four days; 1 after an operation (amputation); 1 after two weeks of moderately restricted diet; 1, who showed renal involvement, after six months of strict diet; 1 after nine months of strict diet with fasting days. In 3 cases it is unknown as to whether the patients were ever sugar-free. One of the fifteen-year cases did not become so until three years before death. There were but 5 of the 62 cases who entirely disregarded treatment, and of these 3 are dead. Among the ten-year cases of 1912 it was recognized that 55 of the 67 had received distinctly better treatment than the average diabetic patient.

In order to determine the quantity of protein per day which the patients were accustomed to eat, analyses of nitrogen in the twenty-four-hour amounts of urine of 19 cases were made. Six of these patients are now dead. Two of these fatal cases, when first seen, had a urinary nitrogen output above 21 gms. The urinary nitrogen of the remaining 4 varied between 13.8 gms. and 15 gms. These are high urinary nitrogens for elderly individuals. Among the 13 cases who are now living but a single one was found who showed as high as 21.5 gms. of urinary nitrogen. The only patients with urinary nitrogens less than 10 gms. are those patients who have been in the hospital on a very low diet. One of these is a patient who had been practically sugar-free for a year. Her nitrogen falls as low as 6 gms. The conclusion can be safely drawn that the protein in the diets of these cases of diabetes living fifteen or more years was usually not far from 75 gms., and the statement is also probably warranted that these patients had never lived long on a high protein-fat diet.

Blood-sugar determinations were carried out in 17 of this series of 62 cases. The results are shown in the following table:

TABLE III.—THE BLOOD SUGAR IN CASES OF DIABETES OF FIFTEEN YEARS' DURATION.

Case No.	Blood sugar, per cent.	Case No.	Blood sugar, per cent.
18	0.09	919	0.22-0.27
29	0.10	970	0.17-0.24
127	0.22	1007	0.09-0.23
155	0.29	1022	0.15-0.20
177	0.25	1043	0.19
352	0.14-0.27	1106	0.13
435	0.13	1111	0.18
887	0.15-0.43	1167	0.23
904	0.21-0.36		

It will be seen that there are only 2 instances (Cases Nos. 887 and 904) with a blood sugar of more than 0.3 per cent. These values were obtained only a short time before death. There were 3 cases with blood sugars which are normal. Case No. 18, in 1897, had an undoubted diabetes, but has been sugar-free for many years. The diabetes was presumably dependent upon gall-stones, and with the disappearance of symptoms of gall-stones the diabetes apparently vanished. A roentgen ray, however, shows caleuli at the present time. The second of these cases, Case No. 29, has continued to do a large amount of work requiring unusual mental responsibility, and although he frequently shows sugar, he rarely shows any great amount. This case is further complicated by a genito-urinary condition which requires frequent manipulation, and the trauma from this may account for the occasional appearance of glycosuria. The other case (Case No. 1007), with the normal blood sugar, presented this after she had been virtually sugar-free for a year. At the beginning of the period the blood sugar was 0.23 per cent. She dieted with great care throughout this year, and only rarely did glycosuria appear. At the period during which the blood sugar was 0.1 per cent., she underwent without disturbance a pelvic operation. Recently this patient had an attack of gall-stones, hitherto unsuspected, but the sugar in the urine did not return and the blood sugar rose only to 0.12 per cent. Now, twenty-one days after the attack, she is sugar-free, and upon a diet of 56 gms. carbohydrate, 57 gms. protein, and 84 gms. fat.

The blood lipoids were determined in 9 of the cases. The results constitute a part of the series of cases studied by Dr. W. R. Bloor and Dr. Horace Gray. In the following table the average figures for lipoids expressed in grams per 100 c.c. blood for the cases which have lasted fifteen or more years are contrasted with the average figures for diabetics of varied duration, and also with Bloor's average figures for normals.

TABLE IV.—THE BLOOD LIPOIDS IN CASES OF DIABETES OF FIFTEEN YEARS' DURATION.

	Total fatty acids.			Lecithin.			Cholesterol.		
	Whole blood.	Plasma.	Corpuscles.	Whole blood.	Plasma.	Corpuscles.	Whole blood.	Plasma.	Corpuscles.
Average value for 0 cases of 15 years' duration	0.62	0.63	0.53	0.33	0.26	0.42	0.25	0.28	0.21
Average value for 105 determinations on diabetics of varied duration	0.80	0.95	0.55	0.36	0.32	0.41	0.32	0.38	0.22
Normal average	0.37	0.39	0.31	0.30	0.21	0.42	0.22	0.23	0.20

From these figures it is observed that the average for these cases is less than for all the diabetics (105 bloods); on the other hand it is higher than the average for the normal bloods. In none of these cases were there sufficient lipoids to be evidenced to the naked eye—in other words, lipemia did not exist. The fact that the averages are less than those of all the diabetics confirms the rule¹ that the greater the duration of the diabetes the less the lipoids are increased above normal. This seems reasonable, for in general a high lipid blood content spells disaster. The following two analyses of the blood of one patient made a year apart show a very definite increase in the amount of total fatty acids and of cholesterol. During this year the patient has been in much better health than at any time formerly, although in order to remain sugar-free she has been obliged to diet very carefully. Her tolerance now, however, is in the neighborhood of 75 gms. carbohydrate, 60 gms. protein and 90 gms. fat, making a total of 1350 calories, or 28 calories per kilogram body weight. Her blood sugar amounts to 0.12 per cent.

TABLE V.—TWO ANALYSES OF BLOOD LIPOIDS OF CASE NO. 1007.

Date.	Total fatty acids.			Lecithin.			Cholesterol.		
	Whole blood.	Plasma.	Corpuscles.	Whole blood.	Plasma.	Corpuscles.	Whole blood.	Plasma.	Corpuscles.
February, 1910	0.40	0.40	0.40	0.30	0.20	0.41	0.20	0.20	0.20
February, 1917	0.45	0.48	0.42	0.27	0.24	0.30	0.22	0.23	0.21

It is encouraging to record the severe illnesses which these 62 cases have survived. Three cases have withstood pneumonia, 8, or 13 per cent., have had gall-stones. Among the 1187 cases the

¹ Bloor, Gray and Joslin: *Jour. Am. Med. Assn.*, 1917, **Ixix**, 375.

incidence of gall-stones was 2 per cent. In some of the cases these were diagnosed prior to the discovery of the diabetes. In others the diagnosis was made subsequently. It should be remembered, however, that gall-stones take years to form, and undoubtedly exist long before they are suspected. One case was operated upon for appendicitis, 2 for fibroids, 2 had ulcers on the leg, gangrene was survived in 4, with 2 amputations, renal complications occurred in 7, and herpes zoster, phlebitis, neuritis, and psoriasis each appeared in at least 1 case. Ten of the patients (4 living and 6 dead) prior to their last illness withstood a considerable acidosis, but in 11 others it was the cause of death. Acidosis, however, was seldom severe. Among those cases in which the twenty-four-hour urine was obtained there was only one patient who had sufficient evidence of acidosis to warrant a determination of the urinary ammonia. In 4 of these cases it was sought and found to be normal. Case No. 310 had a severe acidosis from which she recovered three months before death. Case No. 887, a fatal case, excreted 3.7 gms. of ammonia when first seen. This later rose to 4.7 gms. ammonia while fasting. This case has been reported elsewhere in detail.² It is one of the cases in whom we probably caused acidosis by our former method of treatment, and has been one of the important factors in influencing us to avoid strict fasting in cases which have not been accustomed to such treatment. The other two cases with high ammonia excretions recovered from their acidosis.

The carbon dioxide in the alveolar air was determined in 7 cases. In only one of these was the tension as low as 29 mm. Hg. at entrance to the hospital. Two of these cases died while at the hospital; one of these was Case No. 887, above cited, who showed 29 mm. Hg. tension at entrance. The alveolar air remained at 29 mm. Hg. until twenty-four hours before death, when it suddenly dropped to 14 mm. Hg., from which level it never rose. The other patient, Case No. 904, had a severe carbuncle at entrance and no acidosis. His alveolar air varied from 32 to 38 until seven days before death, when, overcome by his infection, he failed rapidly, and two days before death his carbon dioxide tension was 16, and one day before death 14.

The causes of death of the 25 fatal cases were as follows:

Coma	11
Arteriosclerosis	7
Nephritis	3
Cancer	1
Cystitis	1
Tonsillitis	1
Cirrhosis of liver	1

The 11 cases dying of coma (44 per cent.) make approximately the same percentage as that found with the ten-year series of cases.

² An Analysis of 14 Cases of Diabetes Mellitus Unsuccessfully Treated by Fasting, Boston Med. and Surg. Jour., 1916, cixxv, 425; also The Treatment of Diabetes Mellitus, 1917, 2d ed., p. 359. Lea & Febiger, Philadelphia.

This contrasts very favorably with the 60 per cent. of deaths due to coma in the 1187 cases, but it shows that if acidosis is prevented these patients could be reasonably expected to live for a longer time. The causes of death of the remaining patients may very well have been independent of the diabetes. Today we feel that the deaths of probably 7 of the patients who died of coma could be postponed.

The diabetes is now a minor issue with the patient in 18 of the 37 living cases. Some of these individuals have, it is true, severe nephritis, but 17 are continuing their regular occupations. The diabetes was also a minor issue at the time of death in 7 of the fatal cases. Four of the living cases have outlived their normal expectation of life for their age at the onset of their diabetes. Of the fatal cases 5 outlived the normal expectation of life; in fact, 15 per cent. of the entire series achieved their fulness of years. Ten of the 62 cases were considered severe at the time of the first visit, and now must be regarded on the border-line of severe and moderately severe diabetes; 27 were moderately severe and 24 were mild. One case, when first seen, was considered moderately severe, but later became mild.

CONCLUSIONS. 1. In a series of 1187 cases of diabetes, of whom 1156 are traced, 640 are living and 516 are dead; among these were 62 who lived fifteen or more years, or 5 per cent., and of these 37 are living and 25 are dead.

2. Obesity is universal in the long-lived diabetic. It was demonstrated in 60 cases out of 62.

3. A diabetic heredity is one and one-half times as frequent among the cases of fifteen or more years' duration as among all the diabetic patients.

4. The average loss of weight when the patient first came to us for treatment was 41 pounds.

5. Gall-stones were recognized in 8 cases, being six times as frequent among these cases as in the entire series of 1187 cases.

6. The presence of acidosis was demonstrated 21 times and 11, or 44 per cent., of the fatal cases succumbed to it. By the avoidance of acidosis the lives of these patients might have been prolonged.

7. Arteriosclerosis occurred in 36 cases, and was a prominent factor in causing the death of 10 patients.

8. Diabetes is now a minor issue in 50 per cent. of the living patients, and at the time of death was a minor issue in 28 per cent. of those who had died. An extremely rigid diet is necessary for only 4 of the patients now living.

9. Of the fatal cases, 20 per cent. outlived the normal expectation of life for their age at the onset of their diabetes, and this is already true for 10 per cent. of the living cases.

10. Dietetic treatment was carried out to a considerable degree by 57 cases. Of the remaining 5 cases, 3 are among the dead.